

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
 Organization  
 International Bureau



(43) International Publication Date  
 8 July 2004 (08.07.2004)

PCT

(10) International Publication Number  
**WO 2004/057031 A3**

(51) International Patent Classification<sup>7</sup>: **C12Q 1/68, A61K 45/06**

(21) International Application Number:  
**PCT/IB2003/006419**

(22) International Filing Date:  
 19 December 2003 (19.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
 02293199.2 20 December 2002 (20.12.2002) EP

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): CLIN-IGENETICS [FR/FR]; 1105, avenue Pierre Mendes France, F-3000 Nîmes (FR).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): MARGUERIE, Gérard [FR/FR]; 68, rue du Génie, F-94400 Vitry-sur-Seine (FR). BENHABILES, Nora [FR/FR]; 61, boulevard de Sébastopol, F-75001 Paris (FR).

(74) Agents: BRESSE, Pierre et al.; 3, avenue de l'Opéra, F-75001 Paris (FR).

**Published:**

- ~~with international search report~~
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:  
 12 August 2004

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: METHODS FOR IDENTIFYING THERAPEUTIC AGENTS OF ATHEROSCLEROTIC PLAQUE LESIONS

(57) Abstract: The present invention relates to a method for identifying therapeutic agents for reducing and monitoring the growth, erosion, rupture or stability of an atherosclerotic plaque comprising the analysis of the differential expression of at least two genes coding proteins chosen among Stearoyl CoA desaturase, Phosphatidic acid phosphate, and Phosphoinositide-specific-phospholipase-B1, eventually in association with the analysis of the differential expression of at least one gene coding a protein chosen in the group comprising Aldose reductase and aldehyde reductase, Sphingomyelinase, Acid ceramidase, Ceramide glucosyl transferase, Sphingosin phosphate liase, Thymosine beta 4, Aldehyde dehydrogenase, ATPase Ca<sup>++</sup> binding protein and CD163.

WO 2004/057031 A3

## INTERNATIONAL SEARCH REPORT

national Application No

PCT/IB 03/06419

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68 A61K45/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, MEDLINE, BIOSIS, EMBASE, SEQUENCE SEARCH

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01/62954 A (UNIV BRITISH COLUMBIA ;XENON GENETICS INC (CA); WISCONSIN ALUMNI R) 30 August 2001 (2001-08-30) page 5, line 15-21 page 5, line 26-29 page 6, line 28 -page 7, line 3 page 19, line 17-19 page 23, line 20-24 page 24, line 18,19 page 31, line 15-18 page 49, line 20-25 page 63, line 26-32 --- -/--	1-20

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

8 June 2004

Date of mailing of the international search report

16/06/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Helliot, B

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/IB 03/06419

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 02/063005 A (TOWNLEY DAVID J ;EMERLING BROOKE M (US); HAFALIA APRIL J A (US); I) 15 August 2002 (2002-08-15) claims 20,22,23,25,48 page 25, line 20-23 page 36, line 26,27 page 37, line 6-9 page 51, line 23,24 table 2 claim 22	1-20
Y	US 5 756 291 A (GRIFFIN LINDA ET AL) 26 May 1998 (1998-05-26) table 1	19,20
A	US 6 114 114 A (SEILHAMER JEFFREY J ET AL) 5 September 2000 (2000-09-05) tables 1-4	1-20
P,X	US 2003/166903 A1 (INCYTE GENOMICS, INC) 4 September 2003 (2003-09-04) the whole document table 1	1-20
P,X	US 2003/157082 A1 (MILLENNIUM PHARMACEUTICALS, INC) 21 August 2003 (2003-08-21) the whole document	1-20
P,X	US 2003/153018 A1 (MILLENNIUM PHARMACEUTICALS, INC) 14 August 2003 (2003-08-14) the whole document	1-20

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB 03/06419

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 21  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 21

Present claim 21 relates to the use of a compound modulating the expression of at least two gene coding a protein chosen among stearyl CoA desaturase, phosphatidic acid phosphate and phosphoinositide-specific phospholipase B1.

However, in the absence of any indication as to the nature of the used compound (i.e. the application does not contain any example of compounds according to claim 21), a lack of clarity within the meaning of Art. 6 PCT arises to such an extent that a meaningful search of the claim is impossible.

Consequently, no search has been carried out for the said claim 21.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 03/06419

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0162954	A	30-08-2001	AU 4722801 A CA 2398940 A1 DE 1315831 T1 EP 1315831 A2 JP 2003533978 T WO 0162954 A2 US 2003157552 A1	03-09-2001 30-08-2001 19-05-2004 04-06-2003 18-11-2003 30-08-2001 21-08-2003
WO 02063005	A	15-08-2002	CA 2437497 A1 EP 1358329 A2 WO 02063005 A2 US 2004086905 A1 EP 1241281 A1	15-08-2002 05-11-2003 15-08-2002 06-05-2004 18-09-2002
US 5756291	A	26-05-1998	NONE	
US 6114114	A	05-09-2000	US 5840484 A AU 688465 B2 AU 1694695 A BG 100751 A BR 9506657 A CA 2182217 A1 CN 1145098 A CZ 9602189 A3 EE 9600097 A EP 0748390 A1 FI 962987 A HU 75550 A2 JP 9503921 T LV 11696 B NO 963151 A OA 10723 A PL 315687 A1 WO 9520681 A1 US 6303297 B1 US 2003040615 A1	24-11-1998 12-03-1998 15-08-1995 31-07-1997 16-09-1997 03-08-1995 12-03-1997 14-05-1997 16-12-1996 18-12-1996 26-09-1996 28-05-1997 22-04-1997 20-08-1997 27-09-1996 04-12-2002 25-11-1996 03-08-1995 16-10-2001 27-02-2003
US 2003166903	A1	04-09-2003	NONE	
US 2003157082	A1	21-08-2003	WO 03065006 A2	07-08-2003
US 2003153018	A1	14-08-2003	WO 03045229 A2	05-06-2003